Section 11

Colloids versus crystalloids for fluid resuscitation in Dengue fever patients – a review

Dr. Pablo Perel

For WHO Secretariat
Colloids versus crystalloids for fluid resuscitation in Dengue fever patients

Introduction

Dengue fever

Dengue is a systemic viral infection transmitted between humans by mosquitoes, of which the primary vector is *Aedes aegypti*. It is estimated that there are 50 million new infections per year in approximately 100 countries (Simmons 2012).

In a small proportion of Dengue patients a critical phase, characterized by a systemic vascular leak syndrome, occurs. This syndrome is evidenced by increasing hemoconcentration, hypoproteinemia, pleural effusions, and ascites. It is suggested that in patients with Dengue infection, endothelial dysfunction leads to increased vascular permeability which causes hypoalbuminemia (Simmons 2012).

There are no effective treatments available for Dengue fever. Intervention remains largely supportive with fluid resuscitation for hypovolemia being the mainstay of the medical management of critically ill Dengue patients. When it comes to selecting the resuscitation fluid, clinicians are faced with a range of options including the choice between colloid and crystalloid solution.

Colloids and crystalloids

Crystalloids are fluids based on a solution of sterile water with electrolytes that can be hypertonic, hypotonic, or isotonic compared to human plasma. The most common crystalloids are 0.9% isotonic saline, and lactated Ringer’s solution.

Colloids are similar to crystalloids but in addition they contain a substance that cannot diffuse through semi-permeable membranes owing to its high molecular weight. Example of colloids solutions are albumin, hetastarches (starches), dextran, and gelatin solutions.

Current practice

Current recommendations for the management of Dengue patients with hypotensive shock include the administration of both crystalloids and colloids (WHO 2009).

A recent systematic review found no evidence that colloids, in comparison to crystalloids, reduces the risk of death in critically ill patients (Perel 2012). Although this review included trials involving patients with Dengue fever it did not report the results in these patients separately.
The purpose of this systematic review was to identify and synthesise all available unconfounded evidence to assess the effect on mortality of using colloids compared to crystalloids for fluid resuscitation in patients with Dengue fever.

**Methods**

**Types of studies**
Randomized controlled trials comparing the effects of colloid and crystalloid solutions. As the comparison between fluid types was based on the effect on mortality, we excluded randomised cross-over trials.

**Types of participants**
Dengue patients who required volume replacement. Neonates and pregnant women were excluded.

**Types of interventions**
The following colloids were considered: dextran, starches, modified gelatins, albumin or plasma protein fraction. There is overlap between albumin given for volume replacement and albumin given as a nutritional supplement. Where the trial was of total parenteral nutrition with or without albumin, we excluded it. Trials in which albumin was given as part of volume replacement guided by colloid osmotic pressure or albumin levels were included. The comparison group should receive crystalloid (isotonic or hypertonic) for fluid replacement. When more than one crystalloid arm was included (e.g. lactated rRinger’s and saline) they were combined to form a single comparison group. Trials in which both groups received blood were excluded. Trials of fluids used for other purposes were also excluded.

**Types of outcome measure**
The outcome measure was all-cause mortality assessed at the end of the follow-up period as scheduled for each trial.

**Search methods for identification and selection of studies**
The Cochrane review ‘Colloids versus crystalloids for fluid resuscitation in critically ill patients’ included trials involving critically ill patients including those with Dengue fever; therefore studies fulfilling our inclusion criteria were selected from within those in the Cochrane review.

The search strategy and selection criteria used for the Cochrane review ‘Colloids versus crystalloids for fluid resuscitation in critically ill patients’ are described below. The search for trials was not restricted by date, language or publication status.

In addition to the studies selected from the Cochrane review, we ran updated searches on the MEDLINE and EMBASE databases. One author (PP) screened this search output for any further studies. Finally, two reviews about fluid resuscitation (Akech BMJ 2010; Jalac 2010) and one
guideline about Dengue (WHO Dengue guideline 2009) were scanned to identify any other eligible studies.

**Electronic searches**

The following electronic databases were searched:

- Cochrane Injuries Group Specialised Register (searched 16 March 2012);
- Cochrane Central Register of Controlled Trials 2011, issue 3 (*The Cochrane Library*);
- MEDLINE (Ovid) 1946 to March, Week 1, 2012;
- EMBASE (Ovid) 1980 to March 2012;
- ISI Web of Science: Science Citation Index Expanded (1970 to March 2012);
- ISI Web of Science: Conference Proceedings Citation Index-Science (1990 to March 2012);
- PubMed (searched 16 March 2012);

All search strategies are listed in full in appendix 1.

**Searching other resources**

The reference lists of all relevant papers and published review articles were searched. Known trialists were contacted to identify any further studies. The online trials registers [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and [www.controlled-trials.com](http://www.controlled-trials.com) were also searched for any additional studies.

**Data collection and analysis**

The Cochrane Injuries Group’s Trials Search Coordinator ran the electronic database searches, collated the results and removed duplicates before sending the list of records to the lead review author (PP) for screening.

**Selection of studies**

The full texts of all potentially eligible records were obtained and independently assessed against the pre-defined inclusion criteria by two authors. We resolved any disagreement by discussion.

**Assessment of risk of bias in included studies**

The risk of bias for each study was assessed according to the extent to which the design of the trial had protected the findings from bias. The assessments were made on the basis of sequence generation, allocation concealment, blinding, incomplete outcome data and selective
outcome reporting. The risk of bias was assessed for the following sources of bias (domains) in each study in accordance with recommendations made in Chapter 8 of the Cochrane Handbook of Systematic Reviews of Interventions (Higgins 2011).

1. Random sequence generation (selection bias).
5. Selective reporting: primary outcomes

**Data synthesis**

Trials were stratified by type of fluid. We planned to calculate risk ratios (RRs) and 95% confidence intervals (CI) for each study, however there were too few events to calculate this measure for most of the included trials.

**Sensitivity analysis**

A sensitivity analysis excluding trials with inadequate allocation concealment was planned but was not conducted due to lack of data provided in the included trials.

**Summary of finding and recommendations**

The overall quality of evidence for mortality was rated according to the recommendations of the GRADE working group. In addition to the risk of bias (or study limitation) domain, the inconsistency of results, indirectness of the evidence, imprecision, and publication bias were considered. Evidence generated from randomized controlled trials starts as high quality but is downgraded if any of the above limitations are present. The quality of the evidence was rated as high, moderate, or low.

**Results**

*Included studies (see appendix 2 with table of included studies)*

Five trials evaluating the effects of colloids versus crystalloids were found. All trials involved children with Dengue shock. Three were conducted in Vietnam, one in the Philippines, and one in Indonesia. Two studies had four comparison arms, one had three arms and two had two arms. Three studies compared dextran with crystalloids, three compared starches with crystalloids, and two compared gelatins with crystalloids.

*Risk of bias of included studies (figures 1 and 2)*

Three included studies were judged to be at low risk of bias for allocation concealment, but the one study that contributed mortality data was judged to be at high risk for this domain. All of the included studies were considered to be at low risk for attrition bias. Due to the
unavailability of the original protocols, the risk of bias for selective reporting was judged to be unclear for all of the studies.

**Figure 1: Risk of bias graph**

![Risk of bias graph]

Judgments about each risk of bias item presented as percentages across all included studies.

**Figure 2: Risk of bias summary**

![Risk of bias summary]

Judgments about each risk of bias item for each included study.

References: - high risk ; ? unclear, + low risk
Effect of interventions

Mortality

Dextran versus crystalloids

No deaths were reported in the three studies that compared dextran with crystalloids.

Starches versus crystalloids

Only one study (Cifra 2003) contributed mortality data. One of the 11 patients allocated to 6% Haes died compared to three of 16 patients allocated to Ringer’s lactate (RR 0.48; 95% CI 0.06, 4.08).

Gelatin versus crystalloids

No deaths were reported in the two studies that compared gelatin with crystalloids.

Cost

Volume replacement with colloids is considerably more expensive than with crystalloids. The International Drug Price Indicator Guide shows that the supplier median price for Dextran 70 (0.0106 US$ /ml) is almost 12 times higher than the one for normal saline (0.0009 US$ /ml). For comparison of products that were not included in this guide, data from other commercial web sites were examined. The 'medical and veterinary supplies' web page (http://www.shopmedvet.com) shows that colloids are almost 16 times more expensive than crystalloids; Hespan (6% hydroxyethyl starch) 500 ml solution bag costs US$ 28.50 compared to 1.79 US$ for a 500 ml solution bag of lactated Ringer's.
Discussion

Overall, the quality of the evidence for the effect of colloids versus crystalloids for fluid resuscitation in Dengue patients included in this systematic review was low. The only study contributing with mortality events was at high risk of bias for sequence generation and allocation concealment. Furthermore, the effect estimate was imprecise due to the low number of events. All of the included studies were underpowered to make any reliable assessment of the effect of colloids compared to crystalloids on mortality in Dengue patients.

All of the included studies reported other physiological or proxy outcomes such as time to stability or recovery from shock and need of rescue volume resuscitation. We pre-specified that we would only include mortality as it is the most clinical relevant outcome and one that is less prone to bias. Most of the other outcomes considered (e.g. time to recovery for shock and days in hospital) are not clinically relevant and are prone to bias. In addition, differences in the reporting of these proxy outcomes would have precluded meta-analysis. Even considering these proxy outcomes from the individual studies, the results were mixed with similar number of studies showing benefit, harm or no difference between colloids and crystalloids (table 1).

A previous systematic review evaluating the effects of colloids versus crystalloids in all critically ill patients included 74 trials, 66 of which reported mortality data. The review found no evidence that resuscitation with colloids reduced the risk of death compared to crystalloids (table 2).

In consideration of the low quality of the evidence included in this review, the broader evidence for the lack of effectiveness of colloids compared to crystalloids in critically ill patients and the higher cost of colloids, there is no justification for the inclusion of colloids for volume replacement in Dengue patients in the WHO List of Essential Medicines.
<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Colloids</th>
<th>Crystalloids</th>
<th>Effect estimate (95% CI)</th>
<th>Direction of the effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cifra 2003</td>
<td>Duration of control of shock (mean hours; SD)</td>
<td>31.3 (32.6)</td>
<td>65.5 (27.8)</td>
<td>-34 (-59 to -9)</td>
<td>Colloids beneficial</td>
</tr>
<tr>
<td></td>
<td>Length of ICU stay (mean days; SD)</td>
<td>3.31 (0.7)</td>
<td>3.55 (0.93)</td>
<td>-0.24 (-0.9 to 0.4)</td>
<td>Uncertain</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>1</td>
<td>3</td>
<td>RR 0.48 (0.06 to 4.08)</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Dung 1999</td>
<td>Haematocrit (mean change and 95% CI)</td>
<td>-12.8 (-9.2 to -16.3)</td>
<td>-6.6 (-3.9 to -9.3)</td>
<td>Not reported</td>
<td>Uncertain</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Ngo 2001</td>
<td>Time to first episode of reshock (mean hours; SD)</td>
<td>15 (6.8)</td>
<td>10 (4.1)</td>
<td>5 (2.9 to 7.1)</td>
<td>Crystalloids beneficial</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Prasetyo 2009</td>
<td>Clinical improvement (pulse pressure &gt; 20 mmHg)</td>
<td>17</td>
<td>18</td>
<td>RR 1.05 (0.16 to 6.7)</td>
<td>Uncertain</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>NA</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Wills 2005</td>
<td>Requirement of rescue colloid</td>
<td>31</td>
<td>40</td>
<td>RR 0.76 (0.51 to 1.4)</td>
<td>Uncertain</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>Only 1 death reported but unclear in which group</td>
<td>NA</td>
<td></td>
<td>Uncertain</td>
</tr>
</tbody>
</table>
Table 2: Summary result of Cochrane review evaluating the effect of colloids versus crystalloids in critically ill patients

**Comparison 1. Colloid versus crystalloid (add-on colloid)**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Deaths</td>
<td>52</td>
<td>9920</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>1.1 Albumin or plasma protein fraction</td>
<td>24</td>
<td>9920</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.01 [0.93, 1.10]</td>
</tr>
<tr>
<td>1.2 Hydroxyethyl starch</td>
<td>21</td>
<td>1385</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.10 [0.91, 1.32]</td>
</tr>
<tr>
<td>1.3 Modified gelatin</td>
<td>11</td>
<td>506</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.91 [0.49, 1.72]</td>
</tr>
<tr>
<td>1.4 Dextran</td>
<td>9</td>
<td>834</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.24 [0.94, 1.65]</td>
</tr>
</tbody>
</table>

**Comparison 2. Colloid and hypertonic crystalloid versus isotonic crystalloid**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Deaths</td>
<td>11</td>
<td>14</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>1.1 Albumin or plasma protein fraction</td>
<td>1</td>
<td>14</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.5 [0.06, 4.33]</td>
</tr>
<tr>
<td>1.2 Hydroxyethyl starch</td>
<td>1</td>
<td>90</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.25 [0.03, 2.15]</td>
</tr>
<tr>
<td>1.3 Modified gelatin</td>
<td>0</td>
<td>0</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>1.4 Dextran</td>
<td>9</td>
<td>1879</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.91 [0.79, 1.06]</td>
</tr>
</tbody>
</table>

**Comparison 3. Colloid versus hypertonic crystalloid**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Deaths</td>
<td>3</td>
<td>38</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>Subtotals only</td>
</tr>
<tr>
<td>1.1 Albumin or plasma protein fraction</td>
<td>1</td>
<td>38</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>7.0 [0.39, 126.92]</td>
</tr>
<tr>
<td>1.2 Hydroxyethyl starch</td>
<td>1</td>
<td>16</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>1.3 Modified gelatin</td>
<td>1</td>
<td>20</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
<tr>
<td>1.4 Dextran</td>
<td>0</td>
<td>0</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.0 [0.0, 0.0]</td>
</tr>
</tbody>
</table>
Appendix 1

Cochrane Injuries Group Specialised Register (searched 16 March 2012)
colloid* or hydrocolloid* or crystalloid*

Cochrane Central Register of Controlled Trials 2011, issue 3 (The Cochrane Library)
#1 MeSH descriptor Plasma Volume explode all trees
#2 MeSH descriptor Fluid Therapy explode all trees
#3 MeSH descriptor Resuscitation explode all trees
#4 (fluid* OR volume OR plasma OR rehydrat* OR blood OR oral) next (replac* OR therapy OR substitut* OR restor* OR resuscitat* OR rehydrat*):ti,ab,kw
#5 (#1 OR #2 OR #3 or #4)
#6 MeSH descriptor Colloids explode all trees
#7 MeSH descriptor Hetastarch explode all trees
#8 MeSH descriptor Rehydration Solutions explode all trees
#9 MeSH descriptor Isotonic Solutions explode all trees
#10 MeSH descriptor Serum explode all trees
#11 MeSH descriptor Plasma explode all trees
#12 MeSH descriptor Plasma Substitutes explode all trees
#13 MeSH descriptor Albumins explode all trees
#14 MeSH descriptor Serum Albumin explode all trees
#15 (colloid* OR hydrocolloid* or crystalloid* OR albumin* OR albumen* OR plasma OR starch* OR dextran* OR gelofus* OR hemaccel* OR haemaccel* OR serum OR hetastarch OR isotonic OR ringer* OR gelatin* OR gentran* OR pentastarch* OR pentaspan* OR hartman OR sodium OR potassium OR saline):ti
#16 (Isotonic next saline next solution*) OR (Blood next substitut*) OR (blood next expan*) OR (plasma next volume next expan*) OR (volume next expan*)
#17 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)
#18 (#5 AND #17)

MEDLINE (Ovid) 1946 to March Week 1 2012
1. exp Plasma Volume/
2. exp Fluid Therapy/
3. exp Resuscitation/
4. ((fluid* or volume or plasma or rehydrat* or blood or oral) adj1 (replac* or therapy or substitut* or restor* or resuscitat* or rehydrat*)):ab,ti.
5. 1 or 2 or 3 or 4
6. exp Colloids/
7. exp Hetastarch/
8. exp Rehydration Solutions/
9. exp Isotonic Solutions/
10. exp Serum/
11. exp Plasma/
12. exp Plasma Substitutes/
13. exp Albumins/
14. exp Serum Albumin/
15. (colloid* or hydrocolloid* or crystalloid* or albumin* or albumen* or plasma or starch* or dextran* or gelofus* or hemaccel* or haemaccel* or serum or hetastarch or isotonic or ringer* or gelatin* or gentran* or pentastarch* or pentaspan* or hartman or sodium or potassium or saline).ti.
16. ((Isotonic adj1 saline adj1 solution*) or (Blood adj1 substitut*) or (blood adj1 expan*) or (plasma adj1 volume adj1 expan*) or (volume adj1 expan*)).ab,ti.
17. or/6-16
18. 5 and 17
19. randomized?ed.ab,ti.
20. randomized controlled trial.pt.
21. controlled clinical trial.pt.
22. placebo.ab.
23. clinical trials as topic.sh.
24. randomly.ab.
25. trial.ti.
26. 19 or 20 or 21 or 22 or 23 or 24 or 25
27. (animals not (humans and animals)).sh.
28. 26 not 27
29. 18 and 28
30. (2008* or 2009* or 2010* or 2011*).ed.
31. 29 and 30

EMBASE (Ovid) 1980 to 2012
1. exp plasma volume/
2. exp fluid therapy/
3. exp fluid resuscitation/
4. ((fluid* or volume or plasma or rehydrat* or blood or oral) adj1 (replac* or therapy or substitut* or restor* or resuscitat* or rehydrat*)).ab,ti.
5. 1 or 2 or 3 or 4
6. exp colloid/
7. exp hetastarch/
8. exp "solution and solubility"/
9. exp isotonic solution/
10. exp serum/
11. exp serum albumin/
12. exp crystalloid/
13. exp hetastarch/
14. exp plasma/
15. exp plasma substitute/
16. exp albumin/
17. exp serum albumin/
18. or/6-17
19. (th or ad or iv).fs.
20. 18 and 19
21. (colloid* or hydrocolloid* or crystalloid* or albumin* or albumen* or plasma or starch* or dextran* or gelofus* or hemaccel* or haemaccel* or serum or hetastarch or isotonic or ringer* or gelatin* or gentran* or pentastarch* or pentaspan* or hartman or sodium or potassium or saline).ti.
22. ((Isotonic adj1 saline adj1 solution*) or (Blood adj1 substitut*) or (blood adj1 expan*) or (plasma adj1 volume adj1 expan*) or (volume adj1 expan*)).ab,ti.
23. 20 or 21 or 22
24. exp Randomized Controlled Trial/
25. exp controlled clinical trial/
27. placebo.ab.
28. *Clinical Trial/
29. randomly.ab.
30. trial.ti.
31. 24 or 25 or 26 or 27 or 28 or 29 or 30
32. exp animal/ not (exp human/ and exp animal/)
33. 31 not 32
34. 5 and 23 and 33
35. (2008* or 2009* or 2010* or 2011*).em.
36. 34 and 35

**ISI Web of Science: Science Citation Index Expanded (1970 to March 2012), ISI Web of Science: Conference Proceedings Citation Index-Science (1990 to March 2012)**

#1 colloid* OR hydrocolloid* or crystalloid*)
#2 (Isotonic NEAR/1 saline NEAR/1 solution*) OR (Blood NEAR/1 substitut*) OR (blood NEAR/1 expan*) OR (plasma NEAR/1 volume NEAR/1 expan*) OR (volume NEAR/1 expan*)
#3 #1 OR #2
#4 (fluid* OR volume OR plasma OR rehydrat* OR blood OR oral) NEAR/2 (replac* OR therapy OR substitut* OR restor* OR resuscitat* OR rehydrat*))
#5 (random*) NEAR/3 (study or trial)
#6 (singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*) NEAR/3 (study or trial)

**PubMed (searched 16 March 2012)**
#1 (((plasma volume[MeSH Terms]) ) OR fluid therapy[MeSH Terms]) OR resuscitation[MeSH Terms]
#2 (fluid* OR volume OR plasma OR rehydrat* OR blood OR oral) AND (replac* OR therapy OR substitut* OR restor* OR resuscitat* OR rehydrat*)
#3 #1 or #2
#4 colloids[MeSH Terms]
#5 (colloid* OR hydrocolloid* or crystalloid* OR albumin* OR albumen* OR plasma OR starch* OR dextran* OR gelofus* OR hemaccel* OR haemaccel* OR serum OR hetastarch OR isotonic OR ringer* OR gelatin* OR gentran* OR pentastarch* OR penta* OR hartman OR sodium OR potassium OR saline)[title]
#6 #4 or #5
#7 #3 and #6
#8 (randomised OR randomized OR randomly OR random order OR random sequence OR random allocation OR randomly allocated OR at random OR randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh]) NOT ((models, animal[mh] OR Animals[mh] OR Animal Experimentation[mh] OR Disease Models, Animal[mh] OR Animals, Laboratory[mh]) NOT (Humans[mh]))
#9 #7 and #8
### Appendix 2

#### Table of included studies

Cifra 2003

| **Methods** | Quasi-RCT (allocation by alternation), allocation concealment not reported  
Blinding not reported  
No loss to follow-up |
|---|---|
| **Participants** | 27 children with Dengue shock syndrome  
Exclusion criteria included: other severe infection, protein-deficient abnormalities, bleeding diathesis, patients who have been given multiple plasma substitutes  
Setting: Philippines |
| **Interventions** | 1. 6% Haes-Steril (n = 11)  
2. Ringer's lactate (n = 16) |
| **Outcomes** | Duration of control of shock  
Recurrence of shock  
Length of ICU stay  
Mortality |
<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT. Allocation concealment with numbered opaque envelopes. Double blind with opaque envelopes in blocks of 10. Fluid masked with black opaque containers. Follow-up to hospital discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Dengue shock syndrome; 50 children aged 5-15 years who had not received IV fluid Therapy during current illness Setting Vietnam</td>
</tr>
<tr>
<td>Interventions</td>
<td>Dextran 70 (n=12) Normal saline (n=12) 3% Gelafundin (n=13) Ringer’s lactate (n=13);</td>
</tr>
<tr>
<td>Outcomes collected</td>
<td>Recovery from shock (pulse pressure $\leq$20mmHg), duration No of episodes of shock Improvements in cardiac output Packed cell volume Requirements for further fluid resuscitation Mortality</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>RCT, opaque envelopes containing only treatment pack number</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------------------------------------------</td>
</tr>
</tbody>
</table>
| **Participants** | 230 children with dengue shock syndrome  
Setting: Vietnam |
| **Interventions** | 1. Dextran 70 (n = 55)  
2. 3% Gelatin (n = 56)  
3. Ringer's lactate (n = 55)  
4. 'Normal' saline (n = 56) |
| **Outcomes collected** | Initial pulse recovery time  
Occurrence of timing and subsequent episodes of shock  
Decrease in hematocrit  
Volume of fluid administered until recovery  
Complications  
Mortality |
| **Methods** | RCT  
Sequence generation, allocation concealment and blinding procedures not reported. No loss to follow-up |
|-------------|----------------------------------------------------------|
| **Participants** | 39 children (aged 1 to 13 years old) with Dengue Shock Syndrome  
Setting: Indonesia |
| **Interventions** | 1. HES 130/0.4 (n=19)  
2. Ringer Lactate (n=20) |
| **Outcomes collected** | Shock recovery  
Mortality |
<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>RCT. Treatment allocation was determined in advance with the use of computer-generated random numbers. To ensure pre-randomization concealment as well as blinding, treatment packs comprising three 500-ml bottles of study fluid, sealed inside specially prepared cardboard containers and identified only by a study number, were supplied to the ward for each patient. No loss to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>512 children with Dengue shock syndrome aged 2 to 15 years Setting: Vietnam</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Children with immoderately severe shock were randomised to the 3 interventions  1. Ringer's lactate (n = 128)  2. 6% Dextran 70 (n = 126)  3. 6% HES 200/0.5 (n = 129) Children with severe shock were randomised only to either of the 2 colloids interventions (This comparison between colloids was not included in this review):  1. 6% Dextran 70 (n = 67)  2. 6% HES 200/0.5 (n = 62)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Requirement for supplemental intervention with rescue colloid Time taken to achieve initial cardiovascular stability Time taken to achieve sustained cardiovascular stability Volume required Change in hematocrit Days in hospital 1 death reported but not specified in which group</td>
</tr>
</tbody>
</table>
References

Articles included


Other references


20